



**Testimony
Before the Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives**

Pandemic Influenza Preparedness

Statement of

Bruce G. Gellin, M.D., M.P.H.

Director,

National Vaccine Program Office

Office of Public Health and Science

Office of the Assistant Secretary for Health

U.S. Department of Health and Human Services



**National
Vaccine
Program
Office**

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Mr. Chairman and Members of the Subcommittee, I am pleased to appear before you today to discuss pandemic influenza and the measures the Department of Health and Human Service is taking to prepare for the next pandemic. As you may have heard from reports from last week's World Health Assembly, many public health experts believe the threat of a pandemic is now greater than it has been in decades. A report issued by the World Health Organization warns that the virus may be evolving in ways that increasingly favor the start of a pandemic. In addition the ecology of the disease and behavior of the virus have changed and are creating multiple opportunities for a pandemic virus to emerge. This is in large part because of the bird flu that is established and now endemic in many different species of birds across Asia. As these bird viruses continue to evolve and spread in animals, the possibility increases that an avian virus will mix with a human virus to cause a novel and easily transmitted influenza strain in humans. Since 1997, the avian flu has continued to evolve and has become increasingly lethal for an expanding number of species, including mammals, not just birds. Over the past year and a half, there have been 97 confirmed human cases of influenza in Asia (Vietnam, Thailand and Cambodia) cause by the H5N1 virus and over half of these people have died from their infection.

Secretary Leavitt has made pandemic influenza a priority area. Just last week, at the World Health Assembly – the annual meeting of Ministers of Health from around the world -- he emphasized his concern about the situation in Asia and the Department's commitment to preparedness. He encouraged global

transparency, expanded surveillance, and timely sharing of information and clinical specimens as part of our global preparedness. Secretary Leavitt also urged international collaboration among developed and developing countries to control the spread of this virus among humans and animals. Further, the Assembly considered a resolution on pandemic preparedness that was offered by the U.S. as a blueprint for action.

In addition, on the national front, the Department has been actively developing and formulating a Pandemic Influenza Preparedness and Response Plan. This Plan describes a coordinated strategy to prepare for and respond to an influenza pandemic. It also provides guidance to state and local health departments and the health care system to enhance planning and preparedness at the levels where the primary response activities in the U.S. will be implemented.

This Plan was released for public comment last summer and, as with all preparedness planning, the specifics of this plan will continue to evolve. HHS will continually be revising and reworking the plan to respond to events such as new research, changing influenza virus strains, and discussions with the many stakeholders – state and local health departments, the health care system, industry and the public.

Given the central role that vaccines play in preventing influenza, one of the critical elements of this Plan is to develop a strategy for sufficient domestic surge

capacity for influenza vaccine production. This will require an ongoing and sustained commitment by HHS.

Because a pandemic is by definition the introduction and spread of an influenza virus to which humans have not previously been exposed, this has major implications for vaccine development and supply. In the setting of a pandemic, it is assumed that the pandemic virus will be a novel strain. First, the majority of the population is likely to be susceptible; immunologic naivety with the pandemic strain is likely to result in the need for a two-dose regimen for effective immunity. Unlike seasonal influenza epidemics, a pandemic could come at any time during the year, and may last longer than a single season such that booster dose(s) may be required to sustain immunity. Perhaps most importantly from a preparedness perspective, the perfect vaccine cannot be prepared far in advance and stockpiled, since the ideal vaccine is one that should be tailored to match the circulating virus

Further, as highlighted by the SARS experience, modern transportation and trade are likely to rapidly accelerate the global spread of influenza. As a consequence, our planning assumptions acknowledge that in a pandemic emergency, there will be worldwide demand for vaccine and vaccine produced outside of the United States may not be available for our use.

We are all keeping a watchful eye on the current situation in Asia while at the same time recognizing that, in recent years, there have also been outbreaks of avian influenza infections in Europe and in Canada associated with human infections cases caused by other influenza subtypes. Therefore, in addition to our concerns about the H5N1 virus in Asia, we acknowledge that a pandemic could be caused by another influenza virus subtype could originate in any country.

Though scientists in 1918 had very little idea of what was happening until it was too late, we have time - and still have time - to prepare for the next global pandemic, and we should consider ourselves warned. As Secretary Leavitt stated at the World Health Assembly, "We are working on pandemic preparedness on borrowed time. When this event occurs, our response has got to be immediate, comprehensive and effective."

I want to assure you that the Department has made this one of its highest priorities and it is a critical component of the Secretary's 500-day plan. Ensuring the ability to meet current annual demand for influenza vaccine, to improve the prevention of influenza disease, and to prepare for an influenza pandemic all require strengthening the influenza vaccine supply in the U.S. Building on the response to the influenza vaccine shortage in the 2004-05 season NIH and FDA have worked to facilitate the clinical evaluation in U.S. populations of an influenza vaccine produced by GSK, and efforts are underway to expeditiously consider a

licensure application such that this influenza vaccine may be licensed in the U.S. for the upcoming season.

Several HHS influenza vaccine supply initiatives have a longer timeline and were developed to address pandemic preparedness needs but which also will be critical to achieving annual influenza prevention goals. The objectives of these initiatives are to secure and expand U.S. influenza vaccine supply, diversify production methods, and establish emergency surge capacity. To support these activities, HHS received \$50 million in FY2004 and \$99 million in FY2005. The President's Budget for FY2006 includes an additional \$120 million to further strengthen this component of the overall pandemic influenza preparedness efforts.

Because influenza vaccine is produced to meet the seasonal demand in the fall, production also is seasonal and embryonated eggs have not been available to manufacturers year-round. Moreover, although some excess supply of eggs may be available to support additional influenza vaccine production or provide security if the flocks that produce eggs for vaccine production are affected by avian influenza or other illness, this excess is limited creating vulnerability to supply disruption. To enhance influenza vaccine supply security, HHS issued a five-year contract to Sanofi-Pasteur of Swiftwater, Pennsylvania, on September 30, 2004 for \$40.1 million. Under this contract, Sanofi-Pasteur has begun to change its flock management strategy to provide a secure, year-round supply of eggs

suitable for influenza vaccine production at full manufacturing capacity. It also will increase the number of egg-laying flocks by 25% to provide contingency flocks in case of an emergency. These eggs may be used to support additional production of annual influenza vaccine in the event of a vaccine shortage. Additionally, this contract provides for production of annual investigational lots of prototype pandemic influenza vaccines, e.g., this summer, Sanofi-Pasteur will manufacture an H7N7 virus vaccine for clinical evaluation.

Diversification of influenza vaccine production methods also will help strengthen the system. Cell culture technology is a well-established vaccine production method for other vaccines such as the inactivated poliovirus vaccine and two companies have registered their cell-culture based influenza vaccine technology in Europe. This production technology does not require eggs as a substrate for growth of vaccine virus, thereby avoiding the vulnerabilities associated with an egg-based production system. It also may be more amenable to surge capacity production when influenza vaccine supply needs to be expanded rapidly such as at the time of a pandemic. Finally, influenza vaccines produced in cell cultures rather than eggs will provide an option for people who are allergic to eggs and therefore unable to receive the currently licensed vaccines.

Secretary Leavitt announced last month that the Department of Health and Human Services issued a five-year contract on March 31, 2005 to Sanofi-Pasteur for \$97.1 million to develop cell culture influenza vaccine technology and conduct

clinical trials, with the goal of obtaining an FDA license for this vaccine. Under this advanced development contract, the company has also committed to manufacturing this vaccine at a U.S.-based facility with a capacity to manufacture 300 million doses of monovalent pandemic vaccine over a one-year period. However, given timelines for vaccine development and clinical trials, and for construction and validation of manufacturing facilities, additional influenza vaccine supply from this source is unlikely to be available for at least five years.

These important steps to strengthen our national influenza vaccine supply through assuring the egg-supply and diversifying and expanding production capacity will be followed this year by additional measures to increase influenza vaccine production capacity and expand the number of influenza vaccine doses made using that capacity. Supported by the pandemic influenza vaccine initiative in the FY'06 budget request for \$120 M, we posted synopses of three additional areas where we believe strategic investments move us toward achieving annual and pandemic influenza vaccine supply goals in the March 17, 2005 edition of FedBizOpps. On April 29, 2005, the first of these requests for proposals was posted, providing support for the development of cell-culture based and recombinant pandemic influenza vaccines.

Whereas building new influenza vaccine production facilities is one approach to expand the influenza vaccine supply, other strategies also can increase the number of influenza vaccine doses produced. Influenza vaccine is manufactured in a series of steps – developing an influenza virus master seed for vaccine

production, inoculating the virus into eggs, growing, harvesting, purifying, splitting, formulating, and filling it into vials or syringes. Improving efficiency at any step in this process can increase the eventual yield and number of vaccine doses produced. Thus, a second area of emphasis will be to support improvements of the manufacturing process to increase overall influenza vaccine production at current manufacturing facilities.

The third area of emphasis will provide support for research and development, leading to licensure of strategies that will stretch the number of vaccine doses produced by decreasing the amount of influenza virus antigen that is needed in each dose. The concept underlying these “dose-stretching” strategies is that by changing either the influenza vaccine or the way its administered, one can improve the immune response to vaccination and provide protection while using less of the vaccine antigen. By using less antigen in each vaccine dose, the number of doses that can be made at any level of production capacity can be multiplied. The two most promising antigen-sparing approaches are either to add an adjuvant – a substance that stimulates the immune response to a vaccine formulation, or administering the vaccine into the skin (similar to the approach used in a skin test for Tb) where large numbers of potent immune cells are located. Both strategies have been evaluated in several clinical trials and have the potential to expand influenza vaccine supply several-fold if they prove effective in further clinical trials and are approved for licensure.

The increases in the FY 2006 President's Budget request will support ongoing activities to ensure that the Nation will have an adequate influenza vaccine supply to respond better to yearly epidemics and to influenza pandemics. While issuing the requests for proposals and completing the contracts is only the first step toward the development of an expanded, diversified, and strengthened influenza vaccine supply, the U.S. is leading the global effort to develop vaccines and vaccine technologies to meet this challenge.

We also recognize the important role of antiviral drugs in stemming a pandemic and for treating patients. The United States has ordered and received delivery of 2.3 million treatment courses of Tamiflu. We are in discussions with Roche, the maker of Tamiflu®, to increase our national reserve of this antiviral.

Unfortunately, the H5N1 virus is resistant to the adamantane drugs, the only other class of anti-influenza drugs.

Stemming the spread of the epidemic will require close coordination between the agriculture and health sectors and among affected countries, donor nations and international organizations dedicated to promoting the health of humans, livestock and wildlife. Detailed joint planning is already underway to develop the proposed budget plan for the \$25 million that was included in the FY 2005 emergency supplemental with the Department of State with HHS focusing on human health projects and USAID focusing on projects on animal health and

related issues. In this way, the two agencies' plans will be complementary, not duplicative.

I was part of the U.S. delegation that attended last week's World Health Assembly and want you to know that this administration and the global health community are working together on this public health threat in anticipation of the next pandemic, be it tomorrow or ten years from now. As Secretary Leavitt told the assembled in Geneva, "There is a time in the life of every problem when it is big enough to see and small enough to solve. For pandemic influenza preparedness, that time is now."

Thank you for your attention to my remarks this morning – and more importantly to the attention that you are paying to this important global public health issue.

I would be happy to answer any questions from the Committee.